Celldex Therapeutics Presents Positive Data from Prurigo Nodularis Phase 1b Study Demonstrating Meaningful Reduction in Itch and Skin Clearing with Single Dose 3.0 mg/kg Barzolvolimab

November 5, 2023

- Response observed as early as week 1 and durable for up to 16 weeks -
- Data support important role for mast cells in the pathogenesis of PN and potentially other chronic itch indications -
- Phase 2 PN study to initiate in early 2024 -
- Conference call to be held on Monday, November 6th at 8:00 am ET to discuss study results -

HAMPTON, N.J., Nov. 05, 2023 (GLOBE NEWSWIRE) -- Celldex Therapeutics, Inc. (NASDAQ:CLDX) today announced data from the Company's Phase 1b study of barzolvolimab in prurigo nodularis (PN). Barzolvolimab is a humanized monoclonal antibody that specifically binds the receptor tyrosine kinase KIT with high specificity and potently inhibits its activity, which is required for the function and survival of the mast cell. Mast cells are believed to play an important role in amplifying chronic itch and neuroinflammation, including in PN. This study is the first to demonstrate that barzolvolimab, a mast cell depleting agent, can potentially be used to treat PN and other chronic itch indications. The data will be presented in an oral presentation during the "Hot Topics" Session at the 12th World Congress on Itch (WCI) 2023 on Tuesday, November 7th by Martin Metz, M.D., Professor of Dermatology and Allergy at Charité - Universitätsmedizin in Berlin. Abstracts accepted for presentation at the meeting were released today.

"Prurigo nodularis is a miserable disease where we desperately need treatment options that offer early and durable relief for our patients by not only reducing the relentless itching but also healing the painful lesions that are the hallmark of prurigo nodularis," said Dr. Martin Metz. "These very promising results demonstrate that barzolvolimab and its novel mast cell depleting mechanism could play a meaningful role in breaking the stubborn scratch/itch cycle of this disease and potentially other itch driven conditions. With a single dose, we were able to elicit remarkable clinical results and look forward to what lies ahead in multi-dose studies."

"Today's exciting results in prurigo nodularis add to our strong body of clinical evidence in chronic urticaria and clearly point to barzolvolimab's significant opportunity to meet the needs of the multitudes of patients with mast cell mediated diseases," said Anthony Marucci, President and Chief Executive Officer of Celldex Therapeutics. "We look forward to advancing this program in a Phase 2 study to start early next year as we also seek to expand our leadership into additional mast cell mediated indications."

PN is a chronic skin disease that causes hard, intensely itchy lumps/nodules to form on the skin. The itching (pruritus) can be intense, causing people to scratch themselves to the point of bleeding or pain, which can form lesions and perpetuate the disease cycle. With limited treatment options available, PN is also associated with significant impact on quality of life including sleep disturbance, psychological distress, social isolation, anxiety and depression. Mast cells are believed to play an important role in amplifying chronic itch and neuroinflammation, including in PN where mast cells are associated with pruritic sensory neurons in PN lesions.

Summary of Barzolvolimab Phase 1b Prurigo Nodularis Study Results

The Phase 1b double-blind, single intravenous (IV) dose study randomized 24 adults (evaluable: n=23 safety; n=22 efficacy) with moderate to severe PN across three arms: (1) barzolvolimab 3.0 mg/kg (n=9), barzolvolimab 1.5 mg/kg (n=7) and placebo (n=8). The primary endpoint of the study was safety; key secondary endpoints include changes from baseline in Worst Itch-Numerical Rating Scale (WI-NRS) & Investigator Global Assessment (IGA). The primary timepoint for evaluation of clinical activity was 8 weeks; patients were followed for safety and efficacy endpoints to 24 weeks. Patients on study generally had moderate to severe disease with mean baselines scores across all arms of 8.6 for WI-NRS and 3.3 for IGA.

- These data show that a single IV dose of 3.0 mg/kg barzolvolimab resulted in rapid and durable reductions in itch and healing of skin lesions in patients with moderate to severe PN and that barzolvolimab was generally well tolerated. A Phase 2 subcutaneous multi-dose study is planned for initiation in early 2024.
- At week 8, the percentage of patients with ≥4-point decrease in WI-NRS was 57% and 43% for the single dose 3.0 or 1.5 mg/kg barzolvolimab arms, respectively, and 25% for the placebo arm; this level of response generally persisted out to week 16. In the 3.0 mg/kg arm, a ≥4-point decrease in WI-NRS reduction was seen as early as the first week and reached a high of 71% of patients at week six which was distinct from both the 1.5 mg/kg barzolvolimab and placebo arms.

% of Subjects with ≥4-point decrease in WI-NRS								
Dose	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8
1.5 mg/kg	0	14	29	14	29	29	29	43
3.0 mg/kg	**14**	**29**	**29**	**29**	**57**	**71**	**57**	**57**
placebo	0	0	13	13	25	38	38	25

- At week 8, 29% of patients achieved clear or almost clear skin according to IGA following a single dose of barzolvolimab

3.0 mg/kg. This effect was noted as early as week 2 (the first clinic visit) and was maintained out to week 12/16. No patients treated at 1.5 mg/kg barzolvolimab or placebo achieved clear or almost clear skin according to IGA through week 8. 2 additional patients in the 1.5 mg/kg arm, 2 additional patients in the 3.0 mg/kg arm and 1 patient on placebo had IGA 0/1 at timepoints between weeks 8 and 24.

% of Subjects with IGA 0/1				
Dose	Baseline	Week 2	Week 4	Week 8
1.5 mg/kg	0	0	0	0
3.0 mg/kg	**0**	**14**	**14**	**29**
placebo	0	0	0	0

- Clinical activity was associated with profound serum tryptase reduction. At the 3.0 mg/kg dose, tryptase was profoundly reduced to, or below, the level of quantification and this level of reduction was maintained at least through 8 weeks. Tryptase reduction was observed in the 1.5 mg/kg arm but to a lesser extent.
- Adverse Events (AEs) were generally mild to moderate in intensity and considered unrelated to treatment. During the initial 8 week observation period in the 3.0 mg/kg dosing arm, as previously disclosed, an anaphylactic reaction occurred in a complicated patient with multiple comorbidities; the event fully resolved without sequelae. Generally, AEs seen during the 24-week follow-up period were consistent with comorbidities commonly observed in the PN population.

Webcast and Conference Call
The Company will host a conference call/webcast to discuss the results on Monday at 8:00 a.m. ET. The event will be webcast live and can be accessed by going to the "Events & Presentations " page under the "Investors & Media" section of the Celldex Therapeutics website at www.celldex.com. The call can also be accessed by dialing (646) 307-1963 or (800) 715-9871 (toll free). The conference ID is 3272134.

About Celldex Therapeutics, Inc.
Celldex is a clinical stage biotechnology company dedicated to developing monoclonal and bispecific antibodies that address devastating diseases for which available treatments are inadequate. Our pipeline includes antibody-based therapeutics which have the ability to engage the human immune system and/or directly affect critical pathways to improve the lives of patients with inflammatory diseases and many forms of cancer. Visit www.celldex.com.

Forward Looking Statement
This release contains "forward-looking statements" made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These statements are typically preceded by words such as "believes," "expects," "anticipates," "intends," "will," "may," "should," or similar expressions. These forward-looking statements reflect management's current knowledge, assumptions, judgment and expectations regarding future performance or events. Although management believes that the expectations reflected in such statements are reasonable, they give no assurance that such expectations will prove to be correct or that those goals will be achieved, and you should be aware that actual results could differ materially from those contained in the forward-looking statements. Forward-looking statements are subject to a number of risks and uncertainties, including, but not limited to, our ability to successfully complete research and further development and commercialization of Company drug candidates, including barzolvolimab (also referred to as CDX-0159), in current or future indications; the uncertainties inherent in clinical testing and accruing patients for clinical trials; our limited experience in bringing programs through Phase 3 clinical trials; our ability to manage and successfully complete multiple clinical trials and the research and development efforts for our multiple products at varying stages of development; the effects of the outbreak of COVID-19 on our business and results of operations; the availability, cost, delivery and quality of clinical materials produced by our own manufacturing facility or supplied by contract manufacturers, who may be our sole source of supply; the timing, cost and uncertainty of obtaining regulatory approvals; the failure of the market for the Company's programs to continue to develop; our ability to protect the Company's intellectual property; the loss of any executive officers or key personnel or consultants; competition; changes in the regulatory landscape or the imposition of regulations that affect the Company's products; our ability to continue to obtain capital to meet our long-term liquidity needs on acceptable terms, or at all, including the additional capital which will be necessary to complete the clinical trials that we have initiated or plan to initiate; and other factors listed under "Risk Factors" in our annual report on Form 10-K and quarterly reports on Form 10-Q.

All forward-looking statements are expressly qualified in their entirety by this cautionary notice. You are cautioned not to place undue reliance on any forward-looking statements, which speak only as of the date of this release. We have no obligation, and expressly disclaim any obligation, to update, revise or correct any of the forward-looking statements, whether as a result of new information, future events or otherwise.

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